

Jensen, Kathleen

From: Jensen, Kathleen
Sent: Monday, January 28, 2013 12:25 PM
To: John Sumpter
Cc: Ankley, Gerald
Subject: RE: Data Needed

Hello Dr. Sumpter,

I have attached the data from our fathead minnow beta-trenbolone study. There are 2 files:

1. Trenbolone Fecundity Data (daily egg counts) - there were 5 treatments plus a control, 3 replicate tanks per treatment each containing 2 males and 4 females; the treatment/replicate data is organized in columns along with time (21 days). The numbers in the cells represent the total number of eggs counted each day. Please note there was one female mortality in tank 0.5 A. I have summarized eggs/day, spawns/female and eggs/spawn at the bottom of the worksheet.

2. Trenbolone Endpoint Data - data collected at termination of the study on a per fish basis: vitellogenin, plasma steroids (E, T, 11-KT), GSI, and tubercle score. This file also contains the fecundity data expressed on a per tank basis.

Please let me know if you have any questions or require additional data.

Good luck!

Kathy Jensen



Trenbolone
Fecundity Data (daily egg counts).xlsx

Trenbolone
Endpoint Data.xlsx

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From: Gerald Ankley/DUL/USEPA/US
To: John Sumpter <John.Sumpter@brunel.ac.uk>
Cc: Kathleen Jensen/DUL/USEPA/US@EPA
Date: 01/24/2013 10:27 AM
Subject: RE: Data Needed

Dear John,

Very nice, as always, to hear from you. It indeed is very wintery here. We had some pretty significant cold this past week--minus 30 F at my house one morning, with about a minus 50 F wind chill. Don't spend a lot of time outside in that!

The experiment you are undertaking sounds very interesting, and we have no problem sharing whatever data you need to facilitate getting things done. I will be asking Kathy Jensen (our "keeper of the archives") to help out with this, but before putting a package together for you, we want to make certain we send exactly what you need. Sounds like you are looking for the fecundity data primarily. Are you interested in other endpoints as well (e.g., weight, tubercle score, plasma VTG/steroids, etc.)? Also, would you like daily fecundity information on a per replicate basis, or something a little less "raw"? etc.

It turns out that we actually used those fecundity data to calculate an EC50 value, as a basis for comparison of the potency of beta- vs alpha-trenbolone. I would imagine that you would like to recalculate using whatever technique(s) your statisticians find appropriate, but I thought I nonetheless would send the paper in which we did this along.

All the best,

Gary

[attachment "Jensen et al.2006.Effects of...pdf" deleted by Kathleen Jensen/DUL/USEPA/US]

From: John Sumpter <John.Sumpter@brunel.ac.uk>
To: Gerald Ankley/DUL/USEPA/US@EPA
Date: 01/24/2013 06:32 AM
Subject: RE: Data Needed

Dear Gary,

I'm on the scrounge: no surprise there, of course. I'm after some 'old' data of yours, if you are happy to provide it. The reason is as follows:

A post-doctoral student of mine, Tamsin Runnalls, spent a couple of years investigating the effects of synthetic progestogens on fish. Unsurprisingly, she found some of them to be very effective at inhibiting egg production. I now have a couple of year's money for her to investigate the effects of simple mixtures of steroid hormones on fish. Equally unsurprisingly, when she tested a mixture of EE2 and levonorgestrel (a very potent synthetic progestogen), the activity of the mixture could be predicted based on the concept of concentration-addition. We now want to test more interesting, but still very simple mixtures, and were considering testing a progestogen and an androgen.

Our mixtures 'experts' here, namely Andreas Kortenkamp and his team, tell us that to be able to mathematically predict the activity of a mixture, dose-response data are required for each individual chemical in the mixture. So, ideally, we need the dose-response data for our chosen progestogen (which will be levonorgestrel) and our chosen androgen. And there lies the problem, because few androgens have been reliably tested for their reproductive effects on fish, and for even fewer is their dose-response data. In fact, as far as I can judge, there is only a single paper containing the data we need, and that is of sufficient quality that I would have complete faith in: your paper (ET and C 22, 1350-1360) on 17 β -trenbolone.

What we need is to know the relative potencies of levonorgestrel and trenbolone, so that we can make (probably) an equi-potent mixture of the two. That is, a mixture of the two steroids based on the ratio of their EC50s (their potencies). At a very rough glance, trenbolone looks to be about 10-fold less potent than levonorgestrel, so we would test a 10:1 ratio mixture. We have dose-response data for levonorgestrel, but not trenbolone. We could use your publication to make a reasonable guess at the EC50, or we could run a dose-response study ourselves, to obtain the necessary data. The latter strategy is both time consuming and expensive. The best strategy would be to analyse your data, to calculate the EC50 of trenbolone (in a test system very similar to the one we would use here). We are working with an excellent mathematician here, Martin Scholze, who knows how to underpin mixtures studies with sound mathematics and statistics. So what I am asking is "would you be able/willing to send me the raw data behind your 2003 paper on trenbolone so that Martin can analyse it in the manner he thinks best, in order to determine the potency of trenbolone relative to levonorgestrel, and then for us to use that data to make our mixture?"

If you could retrieve the data (I realise your study was done over a decade ago), and were happy to send it to me, I can guarantee that we would use it only for what I have said above. Having said that, Martin can tease, often by accident, all sorts of things out of biological datasets that we cannot. For example, he has been analysing some of our past datasets to untangle whether the number of eggs per spawning, or the frequency of spawning, or both were affected when exposure to a chemical reduced egg production. As far as we can tell currently, steroids like EE2 and the progestogens do both, with each contributing approximately equally to the reduced egg production.

That is it. I hope all is well, and that you are, somehow, surviving winter in Minnesota. We have quite a lot, by our standards, of snow here right now. And of course we are hopelessly unprepared for it, so chaos ensues, especially with the transport system.

All the very best,

John.